

REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, claims 1-6, 9-10, 13-16 and 18-22 are pending. Claims 1, 9 and 13 are amended, new claims 18-21 are added. Claims 8 and 12 are canceled without prejudice to renewal.

Claim 1 is amended to set forth a substantially non-aqueous shampoo liquid shampoo composition comprising at least one antifungal agent. Support is found, for example, on page 5, lines 11-17.

Claim 9 is amended to set forth proper antecedent basis and proper Markush group language.

Claim 13 is amended to set forth proper Markush group language.

New Claims 18-9 and 21-22 set forth that the antifungal agent is an azole or an imidazole. Support is found, for example, on page 5, lines 11-17; in Examples 1 and 2 on page 7; and in the formulations summarized on page 11. Ketoconazole and clotrimazole are exemplified azole and imidazole antifungal agents.

New Claim 20 sets forth a substantially non-aqueous shampoo liquid shampoo composition further comprising a foam booster. Support is found, for example, on page 4, line 31 through page 5, line 2.

Rejection under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of Claims 1-6, 8-10 and 12-16 as allegedly being obvious over the combination of U.S. Patent 5,866,152 ("the '152 patent"), PCT Publication WO 87/04617 ("the '617 publication"), and U.S. Patent 6,207,694 ("the '694 patent").

The Examiner alleges that it would have been obvious to prepare compositions of the '152 patent and increase the concentration of the PEG of the '152 compositions to greater than 20% and combine with an antifungal agent for the control of dermal infection. *See*, Official Action mailed on December 10, 2004 at page 3, paragraph 2 and at page 5, paragraph no. 9. This

statement indicates that the Examiner is using the '152 patent as the primary reference. The Examiner alleges that motivation to use higher concentrations of PEG stems from the teaching of the '617 publication which discloses that higher concentrations of PEG can dissolve the active ingredients so that better fungicidal properties are exhibited and that PEG also acts as a penetration enhancer. *See, Id.*

The Examiner expressly admits relying on the '617 patent for the teaching of a higher concentration of PEG and communicates relying on the '694 patent for the teachings of specific antifungal agents in shampoo compositions. *See, Id.* at page 5, paragraph no. 9.

To establish a *prima facie* obviousness, the Examiner must show some suggestion or motivation for one of skill in the art to modify the primary reference or to combine the cited references. M.P.E.P. § 2143.

No motivation or suggestion to combine

Primary reference is rendered unsatisfactory for its intended purpose

If a proposed modification would render a referenced invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. M.P.E.P. § 2143.01.

Here, the '152 patent discloses and claims a shampoo composition comprising pyriproxyfen and methods for controlling ectoparasites (*see*, column 6, lines 15-21 and 33-35 of the '152 patent). The sole purpose of the compositions and methods disclosed in the '152 patent is to control ectoparasites, especially lice (*see*, the abstract, and column 1, lines 4-6 and 21-24).

In order to render the claimed invention obvious, the Examiner has proposed replacing the anti-ectoparasite agent, pyriproxyfen, of the '152 patent compositions with an antifungal agent disclosed in the '694 patent. This proposed modification of the '152 compositions render them unsatisfactory for their intended purpose, because the antifungal agents of the '694 patent are ineffective against ectoparasites. The Examiner's proposed modification of the '152 patent compositions render them unsatisfactory for their intended purpose of controlling ectoparasites.

Impermissible hindsight reconstruction was used to combine the cited references

There further exists no suggestion or motivation in the cited references to combine an antifungal agent in addition to the anti-ectoparasite agent in the compositions of the '152 patent. Applicants respectfully assert that the Examiner has used impermissible hindsight reconstruction to combine completely disparate disclosures with completely disparate purposes and concerns. First, the '152 patent discloses including additional insect-controllable agents (e.g., pyrethroid compounds, insect growth regulators and repellants (*see*, column 2, lines 38-46)). The '152 patent does not even mention, much less teach or suggest, anything about fungal infections or their treatment whatsoever. Second, no suggestion or motivation to combine is found in the '617 publication or the '694 patent either. The '617 publication and the '694 patent disclose compositions and methods for treating hyperkeratotic skin conditions, including fungal infections, and have accordingly developed their formulations with acidifying agents and penetration enhancers to counteract hyperkeratosis, a condition consistently associated with dermal fungal infections but that is not of ubiquitous concern in patients infected with ectoparasites such as lice. Unsurprisingly, neither the '617 publication nor the '694 patent even mention, much less teach or suggest anything about ectoparasites or ectoparasitic infections whatsoever. Absent the Examiner's impermissible hindsight reconstruction, Applicants respectfully assert that there is no suggestion or motivation to combine the disparate disclosures of the '152 patent, the '617 publication and the '694 patent.

The offered rationales to combine the cited references fail

The Examiner has put forth as rationales for combining the disclosure of the '152 patent with the disclosures of the '617 publication and the '694 patent that (i) higher concentrations of PEG can dissolve the active ingredients and PEG acts as a penetration enhancer, and (ii) better fungicidal properties are exhibited. This reasoning fails to provide a legitimate motivation to combine the cited references. First, regarding rationale (ii), those of skill in the art have no suggestion or motivation to improve the fungicidal properties of compositions designed and intended to be used in controlling ectoparasites, such as lice. Instead,

a person of skill in the art would reasonably seek to improve the insecticidal properties of the '152 formulations. As discussed above, there is no suggestion or motivation in any of the cited references to include an antifungal agent in the compositions of the '152 patent in the first instance.

Second, regarding rationale (i), there is no motivation to further increase the concentration of pyriproxyfen in the '152 patent compositions above the upper disclosed value of 5%, because this concentration already delivers the Environmental Protection Agency's (EPA) 1999 established maximum daily reference dose of 0.35 mg/kg/day pyriproxyfen in miniscule volumes.¹ For instance, an adult weighing, for example, 150 lb. (68kg) would receive their maximum acceptable daily intake of a 5% pyriproxyfen formulation in a volume of 476 μ l (0.476ml).² A child weighing, for example, 50 lb. (23kg) would receive the EPA established maximum acceptable daily intake of a 5% pyriproxyfen formulation in a volume of 159 μ l (0.159ml). Because the highest disclosed concentration of 5% pyriproxyfen in the '152 patent delivers the maximum acceptable daily intake of pyriproxyfen in such miniscule volumes, the '152 formulations already need to be diluted to be used for their intended purpose as shampoos to control ectoparasites, such as lice. Therefore, there is no motivation to increase the PEG concentrations of the '152 patent in order to dissolve higher concentrations of pyriproxyfen, because the formulations would only have to be further diluted commensurate with the increased pyriproxyfen concentration in order that treated individuals do not receive more than the EPA established maximum acceptable daily intake doses of this insecticide. There is further no motivation to increase the PEG concentrations of the '152 patent for penetration enhancement of pyriproxyfen, because counteracting hyperkeratosis is not a primary concern when treating an ectoparasite (*i.e.*, lice) infection.

¹ Applicants attach as Exhibit A for the Examiner's reference the Acceptable Daily Intake for pyriproxyfen provided through the Hazardous Substances Data Bank, a part of the National Institutes of Health's TOXNET website at <http://toxnet.nlm.nih.gov>. The calculations are based on the unit conversion that 1 pound (lb.) = 0.454 kilograms (kg). The Household Products Database, also provided through the National Institutes of Health, indicates that in the United States, no household products containing pyriproxyfen are for use on humans (attached as Exhibit B).

² A 5% solution = 5g/100mL or 5mg/100 μ L. The maximum daily intake for an individual weighing 150 pounds (68kg) = (0.35 mg/kg/day)(68kg) = 23.8mg/day. In a 5% solution, 23.8mg is in a volume of 476 μ L.

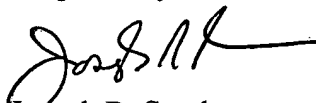
In view of the foregoing reasons, absent impermissible hindsight reconstruction, there is no suggestion or motivation to combine the '152 patent, the '617 publication and the '694 patent. There is certainly no reason to apply the disclosures of the '617 publication and the '694 patent regarding formulations for treating hyperkeratotic skin conditions (*i.e.*, fungal infections) to modify the formulations of the '152 patent, which were developed for the disparate purpose of controlling ectoparasites, such as lice. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,


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PYRIPROXYFEN

CASRN: 95737-68-1

For other data, click on the Table of Contents



Acceptable Daily Intakes:

EPA has established the Reference Dose (RfD) for pyriproxyfen, 2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy] pyridine at 0.35 mg/kg/day. This RfD is based on a NOAEL of 35.1 mg/kg/day and an uncertainty factor (UF) of 100. The NOAEL was established from the combined chronic feeding/oncogenicity study in rats where the LOAEL was 3,000 ppm, based on a 16.9% decr in body weight gain in females when compared to controls. [64 FR 56681 (10/21/99). Available from <http://www.epa.gov/EPA-PEST/1999/October/Day-21/p27398.htm> as of April 28, 2003.]**PEER REVIEWED**

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Chemical Information

Chemical Name: Pyriproxyfen**CAS Registry Number:** 095737-68-1**Synonyms:** Nylar; 2-(1-Methyl-2-(4-phenoxyphenoxy)ethoxy)pyridine; Pyriproxyfen; Pyridine, 2-(1-methyl-2-(4-phenoxyphenoxy)ethoxy)-

Information from other National Library of Medicine databases

Health Studies: [Human Health Effects from Hazardous Substances Data Bank \(HSDB\)](#)**Toxicity Information:** [Search TOXNET](#)**Chemical Information:** [Search ChemIDplus](#)**Biomedical References:** [Search PubMed](#)

Products that contain this ingredient

Brand	Category	Form	Percent
Deep 6 Flying Insect Killer	Pesticides	emulsion	0.10
Enforcer Flea Spray for Homes	Pesticides	liquid	<0.05
Deep 6 Flea Killer Plus Fogger	Pesticides	emulsion	0.10
Bonide Flea Beater Plus 210	Pesticides	liquid	1.3
Zodiac Carpet Powder	Pet Care	powder	0.02
Bio Spot Flea & Tick Control for Dogs over 33 lbs.	Pet Care	liquid	5
Adams Flea & Tick Shampoo with Sykillstop for Dogs & Cats	Pet Care	liquid	0.086
Adams Room Fogger with Sykillstop	Pet Care	aerosol	0.1
Adams Carpet Powder with Linalool and Nylar	Pet Care	powder	0.02
Enforcer Flea Fogger II	Pet Care	aerosol	0.100
Adams Flea & Tick Mist with Sykillstop	Pet Care	pump spray	0.15
Bio Spot Shampoo for Dogs	Pet Care	liquid	0.01
Farnam Fresh & Free Fabric Freshener & Flea Control	Pet Care	pump spray	0.011
Adams Inverted Carpet Spray	Pet Care	aerosol	0.015
Real Kill Indoor Flea Fogger	Pet Care	aerosol	0.100
Enforcer Concentrate for Fleas	Pet Care	liquid	1.30

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EXHIBIT B